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Long-Term Impact of Huntington Disease Linkage Testing

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We performed a long-term follow-up of Huntington disease (HD) predictive testing (an average of 6 years post-test) for 16 of 20 people who received informative linkage test results. Although no pre-test or baseline psychological differences were noted between those with an increased versus a decreased risk of HD, the long-term impact was dramatically different in these two groups. The low-risk group reported less uncertainty, anxiety or worry, fear, and worry about children's risk, whereas the high-risk group reported either the same or increased concern in these areas. Those at low risk also acknowledged an increased sense of control and self-esteem, whereas those at high risk reported decreases or no changes. One high-risk individual reported chronic depression that had occurred since the testing. Additionally, those at low risk reported greater reliance and faith in spiritual or religious beliefs than those at high risk.

The emotional impact of HD genetic testing justifies the continued utilization of pre- and post-test counseling protocols. Pre-test counseling should include discussion of the known risks and benefits of predictive testing, with special emphasis on the participant's expectations for future change and improvement. Although the psychological impact appears mostly favorable for those with decreased risk, there is risk for a decline in psychological well-being over time for those with an increased risk for HD. Am J. Med. Genet. 70:365–370, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: Huntington disease; psychological impact; predictive testing

INTRODUCTION

Huntington disease (HD) is a progressive, neurodegenerative disorder typically of mid-life onset. Symptoms include involuntary choreic movements [Huntington, 1872], cognitive deficits [Moss et al., 1986], emotional difficulties, and changes in personality [Caine and Shoulson, 1983]. HD is an autosomal dominant trait with almost 100% penetrance.

More than a decade ago, a DNA polymorphism linked to the transmission of HD was discovered [Gusella et al., 1983], thereby making a linkage test for HD possible. This test was made available to New England residents who were at risk for HD in September 1986. The cloning of the HD gene early in 1993 [HDCRG, 1993] permitted a direct predictive test which has replaced linkage testing. The direct test is less costly and less time consuming so that many more individuals are now seeking testing. Given the dramatic increase in the number of people being tested, and the potential for adverse consequences, we took this opportunity to examine the long-term impact of predictive testing.

Many studies have examined the attitudes of at-risk individuals toward testing [Kessler, 1987; Mastromauro et al., 1987; Wolff and Walter, 1992] and their partners [Meissen et al., 1991; Jacopini et al., 1992; Tibben et al., 1993a]. Studies of persons at risk for HD indicate that those who predict they may have a depressive reaction or difficulty coping are reluctant to undergo testing [Steenstraten vd et al., 1994; Codori and Brandt, 1994], as are those who are daunted by the lack of a cure, the financial cost and risks, and the finality of a DNA test result [Quaid and Morris, 1993]. Kessler [1987] expressed concern for increased rates of anxiety and depression and increased potential for suicide with a positive result.

Most follow-up studies assessed the impact of testing 6 months to 2 years post-test [Bloch et al., 1992; Huggins et al., 1992; Tibben et al., 1992, 1993b, 1993c; Wiggins et al., 1992], although Codori and Brandt [1994] reported a follow-up study of up to 6 years post-test. Most individuals did not regret being tested [Bloch et al., 1992; Codori and Brandt, 1994], reported less preoccupation with HD [Codori and Brandt, 1994], and reported a decline in depression after 1 year [Bloch et al., 1992; Wiggins et al., 1992]. Additionally, the high-risk group found relief from uncertainty [Tibben et al.,

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1992; Codori and Brandt, 1994], and the low-risk group reported lower psychological distress [Wiggins et al., 1992; Codori and Brandt, 1994].

Testing has not always had benign effects, however. A high-risk result influences the entire family by increasing risk for offspring, increasing burden of care for spouses, and making communication about HD more difficult [Bloch et al., 1992], as well as increasing psychological stress, potential marital difficulties [Codori and Brandt, 1994], and hopelessness about the future [Tibben et al., 1992]. Even some at low risk were challenged when the result was completely unexpected, when irreversible decisions had been made based on being at risk [Huggins et al., 1992], and when there was a lack of positive change after testing [Codori and Brandt, 1994].

The goal of this study was to assess the long-term impact of linkage testing on its participants. The purpose was to:

1) Observe changes made since testing in important life areas, 2) measure the psychological impact of the test, and 3) compare reports between the linkage-positive and linkage-negative groups.

MATERIALS AND METHODS

Predictive testing for Huntington disease was offered through the Huntington Disease Center Without Walls by linkage analysis from 1986 to 1993. (Counseling procedures followed World Federation of Neurology (WFN) guidelines and were published previously [Meissen et al., 1988].) During that time, 65 at-risk persons came to our center to inquire about the test. Twenty-seven of these people completed linkage testing. The other 38 did not complete testing for reasons such as cost, insufficient number of living relatives, or a decision that testing was not right for them. Of the 27 who completed testing, 20 results were informative and 7 were uninformative. Thirteen people were found to be at low risk for inheriting HD (HD–) and 7 were found to be at high risk for inheriting HD (HD+). Of the 20 informative tests, 17 were performed under a research protocol (1986–1988) and 3 were performed as a clinical fee-for-service test (1989–1993).

Standardized psychological assessment (Beck Depression Inventory [Beck et al., 1961], Beck Hopelessness Scale [Beck et al., 1974], Symptom Check List-90-R [Derogatis, 1983], and Schedule of Affective Disorders and Schizophrenia, Life-time Version [Endicott and Spitzer, 1978]) was obtained for all persons before linkage testing. We had previously reported that no differences were found between the HD+ and HD– groups on these scales [Diamond et al., 1992].

A questionnaire and cover letter, which explained the purpose of the survey, were sent to 18 of the 20 people with informative test outcomes in April 1994. One HD– individual was lost to follow-up and one HD+ person died in an auto accident (current residence of the spouse is unknown). Sixteen of the 18 surveys were completed for this study: 5 HD+ and 11 HD–. Ten were returned to us within 2 weeks. Reminders were sent to the 8 remaining individuals after 2 weeks; this brought in 3 more surveys. One HD– person had moved and was never located. Reminders were sent again to the 4 remaining individuals. When no response was received, we called them by phone. In the case of one HD+ person, we contacted a relative but the study candidate never responded to our invitation to participate. Our contact indicated that this individual was having some difficulties which she did not want to discuss including divorce and financial problems. We were successful at contacting the last 3 (all HD+) by phone. All 16 people who received an informative result and completed the survey were included in our analyses. There were no sibs or other relatives within this sample.

The survey was composed of questions on current status and changes since testing in 1) marital status and reproduction, 2) education and occupation, 3) spirituality and religion, and 4) mental health and test attitudes. In addition, the survey sampled the impact of testing on psychological well-being. All questions had multiple choice answers. The wording of the inquiry is reported in italics, and the wording of the selected responses is in quotation marks. A copy of the questionnaire is available on request.

No participants in this follow-up are known to be symptomatic and none have been diagnosed since testing. Short-term (3-month) follow-up using the Beck Depression scale on this sample showed that everyone in the HD+ group had some periods of depression, ranging from moderate to severe [Meissen et al., 1988]; half felt some relief because the ambiguity of their risk status had been resolved. Half reported serious reevaluation of long-term goals for career and marriage. The HD– group primarily felt relief at the 3-month follow-up [Meissen et al., 1988]. Funding for systematic neurologic and psychologic follow-ups of those tested has been denied.

Statistical analyses were performed using the SAS computer package (SAS Institute Inc, Cary, NC). Chi-square analyses using Fisher's Exact Test were performed comparing HD+ people with HD– people on characteristics, life situations, and perceived emotional impact of the test.

RESULTS

Data on 16 individuals with informative results were analyzed (Table I). The survey was conducted between April 1994 and June 1995. The average follow-up time was 6 years and ranged from 1 to 9 years since testing. The follow-up time since testing was more than 5 years for 13 of the 16 participants in our sample, including all those who were HD+. At the time of testing, individuals ranged from 23 to 45 years of age, with a mean age of 32 years. Although the HD+ group was younger (mean, 28 years) than the HD– group (mean, 34 years), the difference was not statistically significant.

Marital Status and Reproduction

At the time of testing, 10 persons were married, 4 were single, and 2 were divorced. Table I shows that 5 individuals had a change in their marital status since the time of testing. Two divorced (1 HD+ and 1 HD–) and 1 single person (HD–) was married, 1 was divorced

TABLE I. Study Participants*

	HD+ (n = 5)		HD– (n = 11)	
Test age	X = 28.0		X = 33.9	
Years since being tested	X = 7.0 Range [6–9]		X = 5.6 Range (1–8]	
Sex (F/M)	3/2		8/3	
	Yes	No	Yes	No
Currently married	3	2	9	2
Change in marital status since test	2	3	3	8
Currently have children	3	2	10	1
Have had children since test	2	3	2	9
Have 4 or more years of college education	2	3	6	5
More education since test	3	2	2	9
Have received an advanced degree since test	2	3	2	9
Currently employed	3	2	8	3
Stopped employment since test	1	4	0	11

*No statistically significant differences were found between the HD+ and HD– groups.

(HD–), and 1 single person was married and separated by the time of follow-up (HD+).

Eleven of 13 persons who reported having children had children before testing. After the test, 4 of 16 people chose to have children, including one who already had some (see Table I). One of the HD+ individuals had prenatal testing for 3 pregnancies and the other did not have prenatal testing for 2 pregnancies. No other prenatal tests have been performed in our program. In addition, the one HD+ individual who died in an auto accident had a child without prenatal testing.

Education and Occupation

Five persons obtained further education after testing (see Table I). Four completed graduate degrees (3 masters and 1 doctorate). A higher proportion of the HD+ group (3/5) sought more education after testing than of the HD– group (2/11).

Eleven persons were *currently employed,* although 7 of them had changed jobs since the time of testing. Of the 5 who were not employed, 4 stopped working prior to testing and 1 after the test. There were no differences between HD– and HD+ outcomes with regard to cessation of employment.

Spirituality and Religion

Significant differences were found between the HD– and HD+ groups in the area of religious and spiritual beliefs and reliance. All 11 HD– individuals *believe in a God* either "absolutely" or "strongly," whereas 4/5 of the HD+ group believe only "somewhat" or "not at all" ($P = .003$). Eight of the HD– individuals *attend a place of worship* "on a regular basis," whereas only one HD+ person does.

Two individuals reported a change in their *belief in God* since testing; one HD+ person reported a "decrease," whereas one HD– person reported an "increase" in belief. Two HD– individuals reported an "increased" *association with a faith* since testing. Three HD– people also "increased" their *attendance at a place of worship* since testing.

Ten of the eleven HD– individuals felt that their *spiritual/religious beliefs* were either "extremely" or "very important" *in helping [them] to deal with the HD test results at the time the results were given,* whereas only 2 of the 5 HD+ individuals felt this way ($P = .06$). Nine of 11 HD– individuals reported that their *spiritual/religious beliefs* were either "extremely" or "very important" *in currently helping [them] to deal with the HD test results,* whereas only one HD+ person reported this ($P = .04$).

Mental Health and Test Attitudes

Since taking the test, 7 people (4 of whom were HD+) reported seeking help from a mental health professional. Eight reported being *depressed for 2 weeks or longer* at some point in their lives. Two were HD+ and 6 were HD–. One HD+ person was hospitalized for depression for 4 days immediately after receiving the results. The HD+ person who died in an automobile accident also had been hospitalized for depression after testing.

Twelve persons, 8 HD– and 4 HD+, reported that "without a doubt," *if [they] could do it over, [they] would still take the test.* Three people, all HD–, reported that they would "probably" or "possibly" *do it over,* whereas one HD+ person said "definitely not." Three people, 2 HD+ and 1 HD–, reported that they did *have an interest in taking the direct genetic test* and wanted information sent; two said they would contact us if they wanted information on testing. The rest reported that they were "definitely not" interested in taking the direct test.

Psychological Impact of Testing

People were asked to report *how [they felt] the results of the HD test affected [their] current feelings and perceptions* of 17 items. People were asked to rank feelings as "increased," "stayed same," or "decreased" since testing. Responses indicating that a *feeling or perception did not exist before or after the test results were given* were coded as "stayed same."

Table II presents *current feelings and perceptions* or long-term changes in unfavorable affects reported since testing. These included *uncertainty, anxiety or*

TABLE II. Psychological Impact of HD Testing on Unfavorable Feelings†

	HD+ (n = 5)				HD– (n = 11)				
	INC	Same	INC + Same	DEC	INC	Same	INC + Same	DEC	*P* values
Uncertainty	1	4	5	0	0	1	1	10	.00*
Anxiety or worry about HD	3	1	4	1	0	0	0	11	.00*
Depression	1	4	5	0	0	5	5	6	.09
Anger	1	4	5	0	2	5	7	4	.25
Fear	1	3	4	1	0	2	2	9	.04*
Regret	1	4	5	0	1	4	5	6	.09
Guilt	1	3	4	1	0	8	8	3	1.00
Thoughts about suicide	1	4	5	0	0	9	9	2	1.00
Worry about children's risk status	0	4	4§	0	0	2	2	9	.01*
Mental health: professional assistance	2	3	5	0	0	5	5	6	.09

*$P < .05$.
†The "increased" and "same" categories were combined for comparison with the "decreased" category. *P* values represent differences between HD– and HD+ groups. INC = increased; DEC = decreased.
§One person had missing data.

worry about HD, depression, anger, fear, regret, guilt, thoughts about suicide, worry about children's risk status, and need for help from a mental health professional. Decreases were reported in 3 categories in the HD+ group: one person reported less anxiety, one less fear, and one less guilt. Most people with an HD+ result reported that their feelings stayed the same over time. However, 3 of 5 reported that *anxiety or worry about HD* had increased since before testing. In contrast, decreases were noted in every category for the HD– group when compared to feelings prior to testing: 100% reported less *anxiety or worry about HD,* 91% reported less *uncertainty,* 82% reported *less fear,* and 82% reported less *worry about their children's risk status.* Significant differences between the two groups were present in each of these categories. Furthermore, 55% reported less *depression,* 55% reported less *regret,* and 55% reported needing less *help from a mental health professional.*

Table III presents *current feelings and perceptions* or long-term changes in favorable affects acknowledged since testing. Changes in *self-esteem, comfort level with relatives (who have HD, at risk for HD, and not at risk for HD), sense of control, ability to enjoy life, and ability to make decisions* were sampled. Some long-term increases were seen in the HD+ group: 3 reported an increased *ability to enjoy life,* 1 reported increased *comfort level with relatives not at risk for HD,* and 1 reported an increased *ability to make decisions.* Most reported no change over time in *self-esteem, comfort level with [all] relatives, and sense of control.* Increases were seen in the HD– group in all of the categories: 73% reported an increased *ability to enjoy life,* 64% reported an increased *self-esteem,* 64% reported an increased *sense of control,* and 64% reported an increased *ability to make decisions.* Significant differences between the two groups were found for *self-esteem* ($P < .03$) and *sense of control* ($P < .03$).

DISCUSSION

Despite its small sample size, this study has strength in the nearly complete participation of those tested through our center and in the long-term nature of the follow-up, the average duration being 6 years. Only one person (HD+) that we located declined participation. It is our impression that individuals who decline participation in follow-up may be experiencing difficulties they do not want to share. Thus, it is essential that follow-up studies strive for complete ascertainment. This group of tested individuals is well educated and well informed; therefore, they are probably self-selected for their ability to handle a major stress such as testing, as was suggested by other authors [Codori et al., 1994; Kessler, 1994; Mastromauro et al., 1987; Tibben et al., 1993a]. Thus, although this group may not be representative of all persons at risk for HD, it may be representative of that subset of individuals who seek testing.

TABLE III. Psychological Impact of HD Testing on Favorable Feelings†

	HD+ (n = 5)				HD– (n = 11)				
	INC	Same + DEC	Same	DEC	INC	Same + DEC	Same	DEC	P values
Self-esteem	0	5	4	1	7	4	4	0	.03*
Comfort level with relatives									
who have HD	0	5	3	2	4	7	5	2	.25
at risk for HD	0	5	5	0	3	7§	5	2	.51
not at risk for HD	1	4	4	0	2	8§	8	0	1.00
Sense of control	0	5	4	1	7	4	4	0	.03*
Ability to enjoy life	3	2	1	1	8	3	3	0	1.00
Ability to make decisions	1	4	2	2	7	4	4	0	.28

*$P < .05$.
†The "decreased" and "same" categories were combined for comparison with the "increased" category. *P* values represent differences between HD– and HD+ groups. INC, increased; DEC = decreased.
§One person had missing data.

The impact of HD testing was significantly different for persons testing HD+ and for those testing HD–. Most striking was that the HD– group reported an overall decrease in unfavorable feelings and an increase in favorable ones; in contrast, the HD+ group predominantly reported little to no change in both favorable and unfavorable feelings over time. In the long term, the HD– group reported less *uncertainty, anxiety and worry, fear and worry about kid's risk* than the HD+ group. In addition, utilization of mental health services declined for most of the HD– group, but it increased or did not change for the HD+ group.

Hopes of reducing one's uncertainty [Jacopini et al., 1992; Mastromauro et al., 1987] and increasing one's ability to make informed decisions are common reasons for being tested [Meissen et al., 1991; Tibben et al., 1992, 1993a,b; Wolff and Walter, 1992]. Although decreases in uncertainty were reported by other groups after testing [Codori and Brandt, 1994; Tibben et al., 1992], our HD+ group reported no long-term decrease in *uncertainty.* We also found that, in the long term, a *sense of control* was much higher for the HD– than for the HD+ group. Tibben et al. [1993b] also found that those with increased risk gained little sense of control for their future. Thus, some of the major expectations that motivate individuals to seek testing were not realized by most persons who tested HD+.

An increase in *self-esteem* was evident in low-risk individuals, but not in those with increased risk. The childhood environment of at-risk individuals was often stressed by the illness of an HD-affected parent. Family histories of suicide, depression, or other psychiatric disorders often coexisted with HD, increasing the risk for psychiatric morbidity in relatives, regardless of genetic status [Kessler, 1987]. For those with increased risk, shortened life expectancy, decreased probability of achieving life goals, or increased likelihood for burdening family with a potential illness may also have contributed to a lowered self-image.

The individuals in our study reported several changes in their marital, reproductive, and educational status since testing. One third of our participants had a change in marital status, with one person (HD+) reporting that test-associated stress ultimately caused a marital separation. Risks to relationships may be greatest when the couple has not adequately prepared for the result, even when the risk is decreased [Huggins et al., 1992]. Family planning is often cited as a primary reason for HD testing [Tibben et al., 1992,1993a,b; Wolff and Walter, 1992]. However, reproductive decisions were naturally influenced by many factors besides genetic information, because people from both lowered and increased risk groups chose to have children after testing. Pre-test counseling can help a couple identify how a genetic test result might influence their decision to have children. Finally, an HD+ test result may provide incentive to accomplish goals in life sooner, such as advancement in education, because a higher proportion of HD+ than HD– individuals sought further education after testing.

Spiritual and religious beliefs are commonly used for coping with the threat of disease and illness, yet they are often overlooked in assessments of well-being. Health professionals concerned with adaptive strategies may consider assessing the importance of religious and spiritual support for an individual [McKee and Chappel, 1992]. Correlations have been reported between degree of religious belief and psychological well-being [Levin, 1994; Williams et al., 1991]. We found that the HD– group was significantly more *religious/spiritual* than the HD+ group. They reported greater faith, greater reliance on their beliefs for support, and more involvement in a place of worship. Although only 4 people acknowledged a change in their beliefs and religious practices after testing, 3 HD– individuals reported increased faith and 1 HD+ individual reported decreased faith. We are not able to assess whether or not an unfavorable test outcome might induce a decrease in faith and so discourage the use of spiritual support. Because most HD– individuals in this study reported high religiosity and HD+ individuals reported low religiosity, the test outcome confounds our ability to assess whether increased spiritual or religious beliefs lead to improved psychological adjustment.

There is not yet enough information to assess whether or not the prior knowledge of carrier status will assist with psychological adjustment around the time of the disease onset. Disease onset is recognized as a time of maximal stress with increased risk for suicide [Schoenfeld et al., 1984]. It is our impression that persons who learn they are presymptomatic may be increasingly worried about and attentive to possible signs of impairment. These worries may contribute to an increased distress and difficulty in coping with disease onset.

There are three take-home messages for genetic counselors in this study. First, although decreased stress and anxiety is likely for those testing HD–, it is much less likely for those testing HD+. Second, although the test result will affect decisions regarding marriage, family planning, and education, HD risk may be blamed for ambivalence in decision making when other overlooked factors are just as critical. Finally, spiritual and religious beliefs and practices are a common support mechanism, especially for those dealing with issues of disability and terminal illness. Reliance on such support may change with an HD+ result.

To evaluate whether or not the individual has a realistic perception of the potential impact of the HD test, counseling may assess the pre-test expectations of the individual regarding psychological adjustment, life plans, and spiritual support. Does the individual have unrealistic beliefs that the test result will relieve uncertainty and resolve reproductive issues? Pre-test counseling can help the person identify areas in which their expectations for testing may be unrealistic and assist the individual to be more psychologically prepared for any test outcome. The substantial emotional impact of the test in a multitude of life circumstances supports the essential role of pre-test counseling to ensure that the decision to be tested is made with an awareness of the potential risks. We strongly support the testing protocols that have been established through the World Federation of Neurology [1989] and

the Huntington's Disease Society of America [Guidelines, 1994].

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